

Chapter 8

International Collaboration for Global Public Health

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8.1 Introduction

There is a long tradition of global collaboration in biomedicine and public health. Examples range from medical outposts in rural communities run by foreign missionaries (Good 1991) to the early infectious disease programs of the Rockefeller Foundation (Fosdick 1989) and from medical services and training programs for indigenous populations set up by colonial authorities (Marks 1997) to the Pan American Health Organization (PAHO) established by a collective of sovereign governments (Cueto 2007).

Two complementary sets of factors provide context for understanding collaboration in global public health: first, the factors that inform globalization generally and global *health* specifically; second, the factors that shape ethical standards for global health programs generally and global health *research* specifically. Good examples of both factors are reflected in this chapter's case studies.

The opinions, findings, and conclusions of the authors do not necessarily reflect the official position, views, or policies of the editors, the editors' host institutions, or the authors' host institutions.

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8.2 The Rise of Globalization and Global Health

Collaboration in global health, as we know it today, began taking shape after World War II when new laws and institutions were established to govern relations among countries. The war's end was marked by efforts to establish a body that would facilitate peaceful relations among member countries. In 1945, the United Nations (U.N.) was established "to save succeeding generations from the scourge of war" and to "promote social progress and better standards of life" (U.N. 1945). Various U.N. agencies were set up to realize these goals—most prominently the World Health Organization (WHO), founded in 1948 "to act as the directing and coordinating authority on international health work" (WHO 1948).¹ Yet even as these institutions were being established, their ability to encourage international collaboration was hampered in two ways.

First, most low- and middle-income countries (LMICs), which bear the bulk of today's global disease burden, were under colonial rule for the first decade of the U.N.'s existence. Hence, these countries were unrepresented in the new organization. In later years, the principle of self-determination (i.e., the right of "peoples" to govern themselves and choose their developmental priorities) and the efforts of nationalist movements secured political independence and membership in the international community. In effect, the governments of these countries were authorized under international law to represent their populations in relations with other governments, thereby enabling equitable partnerships, even in matters of health.

Second, the escalation of the Cold War in the founding years of the U.N. introduced ideological rivalries into its workings. These rivalries often impeded coordinated actions involving health. For example, the 1950s and 1960s were marked by the superpowers' competitive attempts to eradicate specific (often communicable) diseases (e.g., the United States targeted malaria while the Soviet Union focused on smallpox) (WHO 2008b). This selective, disease-specific vertical approach conflicted with the realization in the 1970s that primary health care was a vital component of a national health system. The latter approach defined "health" broadly, recognizing it as a right and acknowledging the impact of socioeconomic factors on wellness (WHO 1978). The emphasis on primary health care became critical for governments of newly independent countries faced with the task of expanding health systems that under colonial rule had catered to a narrow, privileged segment of the population (WHO 2008a). However, ideological disputes over government's role in society and the policies of the International Monetary Fund (IMF), which favored privatization of certain public services (Stuckler and Basu 2009), neglected the primary health care approach (WHO 2008b). The Cold War also influenced patterns of global health collaboration, particularly among members of feuding coalitions that continued to support ideologic allies (Feldbaum et al. 2010).

¹ Other U.N.-affiliated agencies not directly related to health but influencing collaboration in public health include the International Monetary Fund, World Bank, and World Trade Organization.

The fall of the Berlin Wall in 1989 and the collapse of the Soviet Union shortly thereafter marked the end of the Cold War. These events led more countries to adopt liberal and capitalist principles. Other developments—advances in communications (most notably, the Internet) and greater trade and travel across borders—intensified exchanges among national communities. Collectively referred to as *the process of globalization*,² these changes altered the global context for public health collaboration.

On the one hand, the absence of a drawn-out ideological battle led to constructive deliberation and global action in public health. For example, in 2000, all members of the U.N. General Assembly declared their commitment to achieving eight objectives (the Millennium Development Goals) by 2015—half of which pertained to health. Also significant were widespread efforts to address the HIV/AIDS epidemic through such mechanisms as the Joint United Nations Programme on HIV/AIDS (UNAIDS)³ and the more recently established Global Fund to Fight AIDS, Tuberculosis and Malaria.⁴

On the other hand, the growing influence of liberal and capitalist principles in the global environment of the 1990s affected the extent to which governments (especially those of LMICs) were involved and able to collaborate in public health. These changes included

... an increasing reliance upon the free market; a significant growth in the influence of international financial markets and institutions in determining national policies; cutbacks in public sector spending; the privatization of functions previously considered to be the exclusive domain of the state; and the deregulation of a range of activities with a view to facilitating investment and rewarding entrepreneurial initiative. These trends serve to reduce the role of the state in economic affairs, and at the same time increase the role and responsibilities of private (non-state) actors, especially those in corporate business, but also those in civil society.... (WHO 2002)

Generally associated with neoliberal principles, the changes discussed above have reduced governments' public policy role. These developments notwithstanding, there remain compelling arguments for deliberate and sustained engagement by governments in the interest of global public health. Three are discussed below.

8.2.1 *Collective Health*

The first argument is that even with their reduced profile in national health systems, governments continue to bear primary responsibility for population health. Individual citizens can take responsibility for personal health, but certain health

² Definitions of globalization vary by disciplinary focus. Richard Labonté (2004) describes globalization as “a process by which nations, businesses, and people are becoming more connected and interdependent across the globe through increased economic integration and communication exchange, cultural diffusion (especially of Western culture), and travel.”

³ See <http://www.unaids.org/en/>

⁴ See <http://www.theglobalfund.org/en/>

benefits (e.g., clean air, safe roads, potable water) can be secured only through organized, collective efforts generally involving the exercise of public authority. As such, in the interest of global health, a country's public health institutions should be robust—equipped to protect population health, reduce disease, and administer programs that save money and lives (Frieden and Koplan 2010). This case needs to be made for LMICs especially; otherwise, neoliberal principles guiding globalization may further weaken emergent, poorly governed, or underfunded health systems.

Indeed, the exercise (or failure) of public authority influence all ethical issues presented by the cases in this chapter. In Jensen and Gaie's case, an LMIC government has neither passed legislation nor provided support that would effectively prevent discrimination against citizens seeking HIV services. In Zinner's case, an international aid worker must make difficult decisions about who gets preventive HIV/AIDS treatment in an African community characterized by a neglected, poorly funded health system. In Timms' case, a physician encounters an ethical challenge brought about by the underdeveloped health infrastructure in India, the government's lax enforcement of research regulations, and the substantial influence of large foreign pharmaceutical companies on national policy. In List and Boyd's case, a foreign researcher must decide whether there is an ethical obligation to expose an African government's avoidable failure to prevent a TB medication stock-out. Under question in Millum's case is the degree to which both the U.N. (as a collective body of governments carrying out a humanitarian intervention) and the Haitian government (as the provider of health infrastructure for its citizens) can be held morally or legally liable for a cholera outbreak. In Al-Faisal, Hussain, and Sen's case, a public health expert testifying before a U.N. Commission must weigh in on the extent to which (1) foreign governments are obliged to minimize harm to the health of Syrians and Iraqis when applying sanctions and (2) Syrian and Iraqi governments are obliged to conduct a foreign policy that does not jeopardize the health of their citizens. A U.S.-based researcher grapples in Lee, Kleinfeld, and Glassford's case with the question of whether she can ethically justify publishing a paper based on data obtained from two African countries whose governments have neither institutional review boards nor national research guidelines.

8.2.2 *Coordination*

The second argument favoring active engagement of governments in national health systems is their longstanding ability to enter binding legal agreements with each other and other stakeholders. A government's continued involvement is indispensable to shaping broad-based and sustainable solutions to the challenges of global public health. The broad scope of a government's responsibilities (and authority associated with performing these responsibilities) enables it to coordinate public health efforts involving public, private, and civic institutions. The importance of governmental involvement was crystallized in the words of former WHO Director General, Gro Harlem Brundtland, as the 2003 WHO Framework Convention on

Tobacco Control was being drafted: “Tobacco control cannot succeed solely through the efforts of individual governments, national NGOs (nongovernmental organizations), and media advocates. We need an international response to an international problem” (Bodansky 1999). Tackling one of the world’s leading causes of preventable death (i.e., smoking), the Framework Convention adopts a comprehensive strategy that has been signed by the governments of 168 countries.⁵

With completion of the human genome and development of various technologies to use it, interest in DNA repositories has surged (Kaye et al. 2009). The development and increasing use of biorepositories of DNA, tissues, and other biological materials in institutions worldwide present far-reaching ethical challenges. Some challenges, such as those resulting from the collection and use of dried blood spots (Hendrix et al. 2013) or from regular surveillance like the U.S. Centers for Disease Control and Prevention (CDC) HIV surveillance projects, are recurrent and familiar.⁶ When specimens must be shared in the context of collaborative public health emergency response and planning, the challenges can take on greater urgency. Such emergency collaborative sharing has occurred with virus strains for pandemic influenza planning⁷ and with the sequencing of the SARS coronavirus jointly undertaken by researchers from Canada, Hong Kong, Taipei, the United States, and Vietnam during the global outbreak (Tong et al. 2004). Similarly, the sharing of data and health information has long been a source of ethical and legal commentary and is widely viewed as desirable ethical behavior with demonstrable scientific benefit (Committee on National Statistics 1985; Benkler and Nissenbaum 2006).

8.2.3 Accountability

The third argument supporting government engagement in global public health is based on democratic theory. Put simply, a country’s citizens can hold their governments accountable for failure to meet health commitments. In contrast to governments that are accountable to their entire populations, NGO stakeholders in global health answer to narrower constituencies (i.e., corporations to their stockholders, NGOs to their funders, and foreign health organizations to their home governments). Because public health is of general concern, a level of accountability is essential for the entire health system to function properly. The involvement of governments is, therefore, critical both to ensure the widest participation possible in formulating health policies and to sustain such policies despite shifting interests or diminishing profits of partners.

Setting aside the issue of relative advantages or demerits, the diminished role of governments in global public health—especially governments of LMICs—creates

⁵ See http://www.who.int/fctc/signatories_parties/en/index.html

⁶ See <http://www.cdph.ca.gov/programs/aids/Pages/TOASurv.aspx>

⁷ See <http://www.ip-watch.org/2013/05/27/world-health-assembly-pandemic-flu-framework-clears-committee/>

room for others to enter the field. Entrants include public institutions (e.g., international intergovernmental bodies, governments of emerging economies); NGOs (e.g., development and relief agencies, academic health partnerships, faith-based initiatives); private entities (e.g., corporations, philanthropies, individuals); and hybrid entities that pool resources and expertise from public, nongovernmental, and private stakeholders (e.g., The Global Fund to Fight AIDS, Tuberculosis and Malaria). Each entrant to the global health environment plays a unique role. Some take direct action by providing care, some facilitate and leverage the work of others, and some effect change in policies to cultivate better and closer collaboration. All undertake some form of partnership activity.

Essentially, rather than being merely an instrument of foreign policy and diplomacy or a means to technical aid between governments, collaboration in health has grown into a global endeavor involving many actors and stakeholders (Elmendorf 2010). The declining role of governments in public policy presents special challenges for global public health, and the proliferation of stakeholders makes the formation of partnerships more demanding and critical. As such, effective ethical frameworks that can serve as guides for planning and also as arbiters between competing values are indispensable.

8.3 Ethics Frameworks for Global Health

Complementing this political history has been an equally comprehensive set of approaches, each of which provides a moral foundation for defending actions, policies, and decisions in global health. Foremost among these are principle-based approaches, human-rights frameworks, and social determinants of health (SDH), although other approaches have been suggested (Ruger 2009).

8.3.1 Principles and Benchmarks

The debate arising from the 1997 AIDS Clinical Trial Group Study 076 (ACTG-076) to reduce maternal–fetal transmission of HIV served many purposes. Among the most useful was the attention focused on how ethical arguments are applied to substantive problems in global health (Lurie and Wolfe 1997; Varmus and Satcher 1997). Until then, most bioethical reflection had concentrated on domestic topics, aside from revisions to the *Declaration of Helsinki* and other documents. ACTG-076, however, energized discussion about, among other things, the nature of ethical obligations and commitments to groups, countries, and regions—whether of researchers to research participants, of science to society, or sponsors to host countries (Shapiro and Meslin 2001). Accusations of parachute research and double standards abounded, leading many to rethink the applicability of accepted ethical principles and practices and to consider new contexts. They also questioned whether

researchers, sponsors, or governments owed any continuing obligation of care to research participants at the end of a study. The bioethics principles developed over three decades by Beauchamp and Childress (2009) provided a formidable foundation upon which debates about research and health care could be played out—even in the face of critiques about their adequacy and sufficiency as moral theory (Clouser and Gert 1990). Other principles have been recommended by scholars (Lavery et al. 2007) and organizations (United Nations Educational, Scientific and Cultural Organization [UNESCO] 2005), but even proponents of principle-based approaches recognized that more was needed to meet challenges in emerging areas of science (e.g., public health genomics and transborder studies) (Lavery et al. 2007; Emanuel et al. 2008; Macklin 2008).

Indeed, early in the tenure of the National Bioethics Advisory Commission (NBAC) that later reported on the ethics of clinical trials (NBAC 2001), Ezekiel Emanuel proposed that the Commission review the *Belmont Report* principles. He urged the Commission to adopt a new principle to its canon of bioethics, namely a principle of *community* to accommodate ethical issues arising from the recruitment of groups. Although the Commission did not adopt this principle, Emanuel's proposal has since emerged as one of several benchmarks for assessing ethical acceptability of clinical research in developing countries (Emanuel et al. 2004). More relevantly, the concept of community engagement and participation has taken on a greater role in discussions about the importance of partnerships.

The cases by Timms and by Lee, Kleinfeld, and Glassford illustrate the utility of using ethical principles to frame the unique challenges of global collaboration in biomedical research. Timms raises a critical issue about whether a multinational pharmaceutical company conducting clinical trials in an LMIC is responsible for harms sustained by research participants during its investigations. The ACTG-076 debate has broadened the question of accountability, recognizing that impoverished and poorly educated populations living with underdeveloped regulatory, health, and social service infrastructures must prompt reassessment of a multinational trial sponsor's ethical obligations. Such reassessment has focused, naturally, on measures that prevent exploitation of vulnerable and desperate individuals in LMICs (e.g., appropriate informed consent, vigilant recruitment practices). But it has also raised the question of whether foreign sponsors and researchers have an ethical obligation to the host community or country supplying the large and diverse recruitment pool at comparatively lower cost.

In the case described by Lee, Kleinfeld, and Glassford, a researcher must determine, apart from questions of scientific validity and potential health utility, whether proper informed consent was obtained in the acquisition of data and tissue samples being used for research on which she has been invited to collaborate. These data and specimens were gathered using various consent methods from six African countries, none of which had ethics review boards or national research guidelines. Her collaborator assures her that the consent modalities applied, though varying widely, were appropriate to the settings in which they were used. In deciding whether to coauthor an article based on acquired data, the researcher must consider how (or whether) the requirements of informed consent, a foundational principle of ethical research, can

be met in different global settings, particularly those characterized by cultural or linguistic differences, low health literacy, and absence of regulatory infrastructure.

8.3.2 *Human Rights*

Human rights constitute a compelling ethical framework for global collaboration. Based on an ethical vision discernable in early Greco-Roman writings, these principles matured in the work of such social contract theorists as Thomas Hobbes, Jean-Jacques Rousseau, and John Locke. The modern view of human rights presupposes that all persons, simply for being human, have inherent dignity. This dignity constitutes the normative foundation for people having certain inalienable rights. The terms *inherent* and *inalienable* mean such dignity and rights belong to people naturally and are, certainly, *not bestowed* by a political authority. According to human rights theory, a political authority has no ethical basis for arbitrarily depriving individuals of these rights (not having granted such rights in the first place). But because some needs are common and not all goals can be met individually, people choose to surrender certain rights to a public authority established to ensure these ends are realized. Hence, a government

... exists to ensure the well-being of the individuals who give up certain rights in exchange for certain protections and benefits [...]. The same applies to the community they jointly establish. From this analysis, the traditional roles of government include such things as collective security, the administration of justice, the protection of property and [...] the promotion of the public's health.... (Meslin and Garba 2011)

This theoretical sketch provides a backdrop to the 1948 U.N. *Universal Declaration of Human Rights* (UDHR), the ethical cornerstone of the human rights system since the end of World War II. Using human dignity as its starting point, the UDHR codifies a unified ethical vision for preserving a peaceful and just international order while also emphasizing “social progress and better standards of life” (U.N. 1948). Correspondingly, the UDHR contains rights that are broadly political (e.g., fair trial, free speech, freedom of religion) and others that focus on economic and social conditions (e.g., housing, education, health).

As discussed previously, however, the Cold War introduced ideological rivalries into the U.N., rifts that split the unified ethical vision of the UDHR into two treaties: the International Covenant on Civil and Political Rights (ICCPR) (U.N. 1966a) and the International Covenant on Economic, Social and Cultural Rights (ICESCR) (U.N. 1966b).⁸ The two treaties reflected the priorities of the opposing sides—the ICCPR advocated by the U.S.-led capitalist alliance and the ICESCR championed by the U.S.S.R.-led communist bloc. Having two treaties hindered the deployment of human rights as an effective ethical framework for health collaboration during the latter half of the twentieth century.

⁸Article 12 of the ICESCR codifies the right to health.

As the Cold War abated, the global community adopted a more holistic approach to human rights, including the right to health. This was captured in the 1993 U.N. Vienna Declaration and Programme of Action, a document that reaffirmed human rights as “universal, indivisible, and interdependent and interrelated” (U.N. 1993). The Vienna Declaration laid the foundation for the creation of the Office the United Nations High Commissioner for Human Rights (OHCHR), an agency that oversees the promotion and protection of human rights throughout the U.N. system. Moreover, the U.N. Human Rights Council (HRC),⁹ through its special procedures, appoints independent experts (or “special rapporteurs”)¹⁰ to report on areas of concern, including such health-related themes as food, physical and mental health, adequate housing and extreme poverty, and healthy and sustainable environments.¹¹ As noted previously, this holistic approach was also reflected in the adoption of the Millennium Development Goals (most of which are related to health) and exemplified in the coordinated approach to tackling HIV/AIDS. The health and human rights movement, which gained traction during the global discussion on sexual and reproductive health, firmly took root once health professionals responded to the peculiar challenges of treating HIV-positive people facing discrimination (Gruskin et al. 2007; Mann 1997).

Quite apart from the scarcity of fiscal resources that often plague LMIC governments, other challenges preclude adopting an integrated approach to the right to health. For example, a long-standing argument is that the right to health as codified in the International Covenant on Economic, Social and Cultural Rights attaches to individuals and is, hence, unsuited for effectively achieving public health objectives, goals that by definition focus on population health (Meier 2006). In addition, the proliferation of non-state actors in global health mentioned earlier (e.g., relief agencies, academic health partnerships, corporations, philanthropies) make coordination and accountability about the right to health more demanding. By and large, governments are the sole entities authorized to sign health-related human rights treaties such as the ICESCR. International treaties typically have mechanisms for ensuring that signatories fulfill legal commitments. But as discussed earlier, the diminishing role of governments in national policy and the increasing privatization of public services under globalization (WHO 2002) mean that treaty law will likely play a correspondingly smaller role in global health collaboration. Although the influx of new non-state actors allows stakeholders to partner in innovative ways to address challenges in global health, the stability and accountability of international human rights law remains a valuable asset in a constantly evolving field.

Most cases in this chapter feature ethical issues that are illuminated but sometimes complicated by the human rights framework. In Jensen and Gaie’s case, human rights potentially impede a public health strategy for controlling the spread of HIV/AIDS. The case calls for a public health official to balance the human rights

⁹ Until 2006, the U.N. Commission on Human Rights.

¹⁰ The Human Rights Council also uses working groups.

¹¹ For special procedures of the Human Rights Council, see <http://www.ohchr.org/EN/HRBodies/SP/Pages/Welcomepage.aspx>

of individuals (possibly suffering discrimination and stigma-related violence under routine or mandatory testing policies) against the health of the community, which, arguably, is better served by precisely such testing regimes.

A distinguishing mark of globalization is the increased influence of transnational businesses on the policies of LMIC governments. Timms' case illustrates the impact of this development. Given the economic and political clout of transnational businesses, there are continuing discussions on the extent of their human rights obligations (Weissbrodt and Kruger 2003; Ratner 2001). In this case, even if the pharmaceutical company conducting research in India is not directly bound by a human rights treaty, is it obliged to comply with human rights norms on some other basis (e.g., national laws, industry standards, corporate codes of conduct)?

In 2011, the U.N. Human Rights Council endorsed the *Guiding Principles on Business and Human Rights*, a document outlining what has come to be known as the U.N. "Protect, Respect and Remedy" framework. *Guiding Principles* recognizes governments' duty to *protect* human rights, acknowledges corporate responsibility to *respect* human rights, and requires governments to ensure that people harmed within their jurisdiction have access to effective judicial and nonjudicial *remedies*.

List and Boyd's case questions how one's freedom of expression (Article 19, ICCPR) affects public health. Should one be allowed to use the free press to advocate on behalf of fellow citizens? Does the free press furnish a forum for an informed and representative discussion on public health policy? Are expatriate workers less likely than nationals to face official retaliation when they use media outlets to criticize government?

Conflict in the Balkans and killings in Rwanda in the early 1990s revived lively debate on the international community's obligation to intervene in internal affairs of member countries to defend human rights (Kardas 2010; Chopra and Weiss 1992). Organizing international action to address human rights violations remains a perennial challenge—exemplified by the intractable situation in Syria following major pro-democracy protests in 2011. But ideological alliances and rivalries during the Cold War made consensus building around such interventions arduous (Eisner 1993). The Balkan and Rwandan conflicts and a growing atmosphere of cooperation in the face of global challenges (e.g., environmental degradation, climate change) contributed to an increase in peacekeeping and humanitarian operations organized by the international community. These operations, though designed to further human rights, sometimes undermined the target population's right to health.

Millum's case and that of Al-Faisal, Hussain, and Sen raise issues that result, paradoxically, from increasing adoption of the human rights framework as an international norm. Millum's case questions responsibility during a major cholera outbreak originating in a camp occupied by Nepali soldiers on a U.N. peacekeeping mission in the Caribbean. The Al-Faisal, Hussain, and Sen case considers how the health of vulnerable groups in Iraq and Syria is affected by economic sanctions imposed on the two countries' governments and shows how interventions intended to protect human rights can still have adverse health consequences.

Increasingly, human rights are being used to frame responses to global public health challenges (Adorno 2009; Mann 1997). Human rights are a pervasive transcultural and

normative discourse. Issues once relegated to bioethics are now cast as human rights concerns (Adorno 2009; Faunce 2005). For example, UNESCO adopted three declarations that use human rights to frame health challenges: the Universal Declaration on the Human Genome and Human Rights (1997), the International Declaration on Human Genetic Data (2003), and the Universal Declaration on Bioethics and Human Rights (2005). Each declaration codifies the principle of informed consent—a principle at stake in the case cited by Lee, Kleinfeld, and Glassford and, to a lesser degree, the case by Timms. The cross-fertilization of concepts and concerns between bioethics and human rights is a salutary consequence of public health partnerships forged in an increasingly interconnected and complex world.

8.3.3 *Social Determinants of Health*

The social determinants of health (SDH) framework is based on social justice (Lee 2004). The guiding principle of SDH is *equity*. As with public health, SDH emphasizes population health and prevention. However, SDH goes beyond traditional public health approaches because, in addition to deploying interventions aimed at reducing population mortality and morbidity, SDH targets “the social context and conditions in which people live” (Blas et al. 2011). These contextual factors and conditions that affect health outcomes in a given population are called *social determinants of health*.¹² These include such factors as housing, education, transportation, employment, insurance coverage, and access to health care (Brennan Ramirez et al. 2008).

The SDH framework stands on 40 years of research demonstrating that clinical care alone cannot improve health outcomes unless social factors are addressed (WHO 2007). Statistical associations between social disadvantage and poor health became increasingly clear, impelling the inference that closing the gap in health status between populations required corresponding improvements in the social contexts of disadvantaged populations.

The ethical norm underlying efforts to eliminate these preventable health differences is the principle of equity. Health *inequities* are differences “socially produced; systematic in their distribution across the population; and unfair” (WHO 2007). On the other hand, health *equity* is “the absence of unfair and avoidable or remediable differences in health among population groups defined socially, economically, demographically, or geographically” (WHO 2007). These definitions highlight two aspects of SDH. First, the differences in health are not merely descriptive but prescriptive as well, implying an ethical obligation in favor of their elimination. Second, the focus on social context and conditions means that policy and action must be intersectoral, involving actors and spheres outside the health field (WHO 2007).

¹² The social determinants of health have also been characterized as “the conditions in which people live and work that affect their opportunities to lead healthy lives” (Labonté and Schrecker 2007).

Health disparities among populations in different parts of the world motivate public health interventions and assist the development of useful analytical tools for global health. A case in point would be the gaps in infant mortality rates and life expectancy between countries with strong economies and LMICs. These gaps provide moral stimulus for elimination and benchmarks for setting goals and assessing progress (e.g., the health-related Millennium Development Goals).

The SDH framework faces several challenges and limitations. Most people do not realize the impact of social and contextual factors on health outcomes. Political orientations and worldviews further impede the acceptance of SDH as a viable policy alternative (Gollust et al. 2009). Some argue that variations of SDH oversimplify the link between wealth and health, thereby failing to consider other causes of health disparities (Poland et al. 1998). Even though statistical links have been made between social context and ill health, scientific questions remain on the mechanisms that account for these associations. This is especially critical in the field of mental health, where attempts have been made to clarify associations between SDH and psychological well-being (Marmot et al. 1997; Bovier et al. 2004; Fisher and Baum 2010; Paananen et al. 2013).

Aside from the availability of HIV/AIDS health services and medication, the Jensen and Gaie case and Zinner case demonstrate how social factors affect health. In Jensen and Gaie, advocates of client-initiated voluntary testing (vigilant, rights-based) offer compelling reasons to minimize the potential for discrimination and stigma-related violence against people living with HIV. As the case points out, the risk of violence or discrimination is particularly high in LMIC societies where social, cultural, and legal protections are nonexistent or being developed.

Although HIV-positive status can have adverse social consequences, Zinner illustrates how social factors increase the risk of infection in the first place. In this case, an international anti-AIDS program administering pre-exposure prophylactic medication is deciding whether to budget small sums of money to educate young girls in the community. Investing in education should reduce their likelihood of getting infected in unequal liaisons with older men (sugar-daddy relationships) while creating openings in the program for other at-risk groups to participate. In effect, the program is considering medical intervention (i.e., a pre-exposure prophylactic drug) and social determinants of health (i.e., girl-child education) in making its allocation decisions.

Both Timms' and Lee, Kleinfeld, and Glassford's cases show how social determinants (e.g., gender, caste, economic status, literacy) influence the effectiveness of informed consent for vulnerable LMIC populations participating in drug research. Less direct but equally critical, these cases also show how geographic disparities in social conditions establish context for global health research. The challenge of ensuring that drug research is conducted ethically in LMICs derives from such contextual factors as greater disease burdens in these regions due to underdeveloped health systems, lax regulation of biomedical research due to ineffective governance structures, and economic and social vulnerability of most potential research participants (Barlett and Steele 2011).

In the context of SDH, empowerment "is inseparably linked to marginalized and dominated communities gaining effective control over the political and economic processes that affect their well-being" (WHO 2007). List and Boyd's case demon-

strates how citizens of LMICs can use mass media to influence their governments on public health topics. A physician-national in an East African country fears retaliation if she talks to the media about a TB medication stock-out potentially due to government corruption and misuse of public funds. Her fears underscore the risks and responsibilities associated with the role of health workers as advocates for the socially and politically marginalized in their communities (Pérez and Martinez 2008; Farmer 2004; Geiger and Cook-Deegan 1993). Also pertinent from a global SDH perspective is the likelihood that an expatriate whistleblower, especially a citizen from a higher-income country, would not face as serious a risk.

8.4 Summary

The approaches and methods for collaborating in global public health are diverse—just like the cases in this chapter. These cases reflect the rich and multifaceted context for global public health while also emphasizing the role that different ethical standards (and the foundations for those standards) play. In so doing, the cases offer a fresh and innovative perspective on the ethics of public health.

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8.5 Case 1: The Ethics of HIV Testing Policies

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8.5.1 Background

The global public health community has significantly advanced our understanding of the biology of the human immunodeficiency virus (HIV) and developed reliable diagnostic tests and effective antiretroviral treatments. Despite these advancements, the rate of prevalence and transmission, especially in low- and middle-income countries, remains alarmingly high. HIV prevention, often considered better than a cure,

remains the mainstay of our collective response to the epidemic. By all accounts, HIV testing plays a pivotal role in treatment and prevention, yet in low- or middle-income countries, only 10 % of those who have been exposed to HIV infection may have access to counseling and testing (UNAIDS/WHO 2004; Centers for Disease Control and Prevention 2012). In general, HIV testing policies range from voluntary or client-initiated counseling and testing to provider-initiated approaches (e.g., routine testing, mandatory HIV screening). Most policy makers and health workers have promoted voluntary HIV testing, although routine HIV counseling and testing increasingly is being adopted. Notably, however, the global health community has adamantly discouraged mandatory HIV testing (UNAIDS/WHO 2004).

Resource-poor countries may be unable or unwilling to ensure social and medical infrastructures adequate for safeguarding the human rights of people seeking services. As a result, global health officials have encouraged countries to adopt voluntary or client-initiated counseling and testing policies opposed to routine or provider-initiated policies. Even in settings in which voluntary counseling and testing is readily available, few people take advantage of these services. Stigmatization persists as an obstacle to HIV counseling and testing, which, by all accounts, is vital to effectively treat people living with HIV and AIDS and to reduce further infection.

Many public health ethicists recommend that policy makers and health workers carefully consider the ethical consequences of routine testing policies, especially for people in locales that lack protections against discrimination and stigma-related violence (Rennie and Behets 2006). To protect individuals against HIV-related discrimination and threat of violence, advocates of the human-rights approach vigilantly oppose the application of standard methods of disease control, which include mandatory testing and partner notification. But this vigilant rights-based approach to HIV prevention, an approach that Bayer (1991) labelled AIDS exceptionalism, can undermine society's ability and indeed responsibility to control the epidemic. And although public health officials are a minority, some argue for mandatory HIV testing (Schuklenk and Kleinsmidt 2007), seeing it as the only way to control the HIV epidemic. Failure to apply standard methods of disease control, some argue, devalues public health and social justice (Frieden et al. 2005; De Cock et al. 2002). By treating HIV/AIDS differently than other infectious diseases, AIDS exceptionalism may inadvertently increase stigmatization rather than reduce it (De Cock et al. 2002). Proponents of testing point to its potential to reduce stigma by raising awareness, preventing transmission, expanding treatment, and empowering individuals (Crepaz et al. 2004).

HIV testing policy recommendations from the global international public health community can also challenge if not undermine the authority of the indigenous knowledge system or indigenous ethical codes (Chilisa 2005; Dube 2006; Jensen and Gaie 2010). These recommendations typically stipulate ethical preconditions within voluntary HIV testing policies, such as strict confidentiality, informed consent, and competent pre- and post-test counseling. Some argue that preconditions constitute a Western approach that blocks local efforts to control the epidemic. Although many believe that the context of provider-initiated HIV testing preserves "sufficient voluntariness," others have criticized this approach. Critics maintain that opting-out from provider-initiated HIV testing differs significantly from

client-initiated or voluntary HIV counseling and testing (Kenyon 2005). In either case, all agree, medical practitioners and policy makers cannot guarantee ideal or even adequate social and institutional support services (Weiser et al. 2006).

These disputes are by no means merely theoretical. In Botswana, for example, policy has shifted within the past 5 years from a client-initiated to a provider-initiated or routine HIV diagnostic counseling and testing strategy (Botswana Ministry of Health 2012). More recently, in response to a parliamentary-approved public health bill presently being contested as unconstitutional (Botswana Network on Ethics, Law and HIV/AIDS 2012), the debate has shifted to whether certain conditions render mandatory testing ethically permissible.

8.5.2 Case Description

The Minister of Health of a sub-Saharan nation has asked you, a public health official and physician from a Western country, to recommend an effective HIV testing policy. The sub-Saharan nation is among the hardest hit by the HIV epidemic (e.g., the HIV prevalence rate among pregnant women aged 15–49 is >25 %). In this resource-poor nation, people with HIV and AIDS are commonly stigmatized despite national campaigns to reduce stigma. Even if the nation were to adopt a policy of voluntary HIV counseling and testing, more than 50 % of people living with HIV and AIDS are unaware of their serostatus. Although HIV treatment is currently unavailable, international donors have promised to provide free or inexpensive antiretroviral therapies (ART).

You have sought the input of your colleagues in global public health only to discover they are contentiously divided. Some vigorously oppose enhanced HIV testing policies that would move from voluntary to routine HIV testing to protect the community against discrimination or stigma-related violence. They also oppose in principle Western-based interventions, which, they say, undermine traditional loci of authority and indigenous systems of medical knowledge. Other colleagues insist that human rights-based approaches undermine public health's ability, as well as responsibility, to control the HIV epidemic. They are for moving beyond client-initiated approaches and vigorously support mandatory HIV testing. These colleagues feel that the only way to control the HIV epidemic is to apply the standard methods of disease control.

Given these divergent views, you hope to be able to recommend a HIV policy that strikes a balance between the Hippocratic ideal of doing no harm and the equally compelling mandate to protect if not improve public health.

8.5.3 Discussion Questions

1. How might an emphasis on protecting human rights in HIV prevention reduce the importance of public health and social justice?
2. Is opting in, or not opting out, as part of the routine testing strategy, ethically equivalent to acquiring consent within a voluntary testing site? What are the

necessary and sufficient conditions, ethical or otherwise, for “adequate information” or “sufficient voluntariness” in cases of HIV testing?

3. Is there an ethical conflict between one’s duty, whether as a physician or a public health official, whether as the minister of health or simply as a person, to adopt what are considered to be effective methods of controlling disease, e.g., HIV, and the obligation to respect indigenous knowledge systems and approaches to public health? If there is a conflict, which duty should take precedent?
4. What policy would you recommend under these circumstances? And what ethical principles guided your recommendation?
5. How would your recommendation provide, if at all, protections against discrimination and stigma-related violence?

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8.6 Case 2: Just Allocation of Pre-exposure Prophylaxis Drugs in Sub-Saharan Africa

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8.6.1 Background

During the summer of 2012, the U.S. Food and Drug Administration (FDA) announced the approval of Truvada (emtricitabine/tenofovir disoproxil fumarate) for use in pre-exposure prophylaxis programs (PrEP) for people at high risk of HIV infection (FDA 2012). After successful use of antiretroviral therapy (ART) drugs to treat HIV/AIDS-infected populations, researchers found that daily prophylactic use of these drugs in uninfected individuals who engaged in high-risk activities was also effective in reducing their risk of HIV/AIDS. The U.S. Centers for Disease Control and Prevention (CDC) noted that PrEP could reduce HIV rates for men having sex with men if those at high risk of HIV infection were targeted and if PrEP was used as part of a comprehensive set of preventive services, including regular monitoring of HIV status, adherence, and risk behaviors (CDC 2011). Candidates for Truvada should first be tested for HIV to ensure that they are in fact HIV negative before beginning the PrEP program.

This innovative prophylactic approach to reducing the likelihood of contracting HIV holds great promise. One study found that Truvada reduced the risk of HIV infection 42 % compared with men taking placebos and having sex with other men (Grant et al. 2010), whereas a second study found that risk fell by up to 75 % compared with serodiscordant couples taking placebos (Baeten et al. 2012). However, Truvada is associated with some side effects, including nausea and vomiting (CDC 2011) and possible decreases in bone mineral density (Grigsby et al. 2010).

Furthermore, Truvada is contraindicated for anyone with decreased kidney function. Regular testing of kidney function is recommended for those people taking this medication (CDC 2011).

Truvada has been tested only in serodiscordant couples—not in women. Its efficacy in the general population of women, in sex workers, and in young girls in sugar-daddy relationships (i.e., young girls in unequal relationships with older males) is unknown.

Sub-Saharan Africa has been hit especially hard by HIV/AIDS. An estimated two-thirds of people affected by HIV worldwide are concentrated in this area, although significant variations exist in different parts of the continent (Kalipeni et al. 2004). Unfortunately, the distribution and availability of ART drugs have exposed the inadequacies of some African national health systems, such as the negative effects of a long-neglected health sector, economic challenges, declining public expenditures, and decentralized funding (Schneider et al. 2006).

Many international aid groups help fund public health programs, including programs to reduce the spread of HIV/AIDS. Programs such as PEPFAR (The United States President's Emergency Plan for AIDS Relief), the Global Fund, the World Bank, the United Nations, and the Gates Foundation have all contributed large sums of money for this purpose.

African groups at high risk of contracting new infections (and thus good potential candidates for PrEP) include sex workers, men having sex with men, serodiscordant couples, and girls in sexual sugar-daddy relationships. The latter group poses specific ethical issues. These girls, typically teenagers, may be coerced into sexual relationships with men old enough to be their fathers or even grandfathers through the offering of gifts or money. These sugar daddies generally engage in multiple sexual relationships, possibly with a spouse and several young women, while putting the girls at risk of HIV. Every averted case of HIV increases economic productivity, lowers the risk of social unrest, strengthens the labor force, and improves the investment climate (Over 2011).

8.6.2 Case Description

You are the head of an international anti-AIDS effort currently stationed in a community of 40,000 in sub-Saharan Africa, where the HIV prevalence rate is 21 %. You have received funding from different world organizations, including some based in the United States. Your organization is piloting the use of Truvada in populations that are at high risk of HIV. The organizations funding this project will allow you and the two health workers assigned to assist you to make all allocation decisions.

The cost of Truvada for one patient is about \$500 per year. Those living in this community are poor, and none could afford this drug without the existence of your program. Many populations in the community are at high risk of HIV infection, including homosexual and bisexual men who routinely engage in sex with other men, girls in sugar-daddy relationships, sex workers, and serodiscordant couples. You have been given enough Truvada to treat and monitor 100 patients for a year.

The funding organizations have indicated that they are likely to provide more Truvada if you find its use results in no or few new infections during the year among the 100 selected patients. The community of 40,000 people include the following:

- 80 men who have sex with other men;
- 80 girls in sugar-daddy relationships;
- 40 sex workers; and
- 30 serodiscordant couples (60 people; noninfected partner receives Truvada while the infected partner is not medically eligible for ART).

One challenge you face is that many feminist organizations and child health advocates are pressuring you to include all girls in the group because ample research shows that girls in sugar-daddy relationships are relatively powerless and cannot ask their partners to wear a condom, virtually ensuring that these girls will become infected. There is some evidence, however, that simply paying girls a small amount of money to attend school (and thus dramatically reducing the possibility of these relationships) is cost effective. If you adopt this approach, you could use the Truvada for the other groups. You may need to consider whether to request more money from the funding organizations if you adopt this approach. One of your organization's goals is to respect cultural norms and beliefs if the health of those at risk of HIV/AIDS is not jeopardized. You have been asked to allocate the PrEP drugs in your community.

8.6.3 Discussion Questions

1. What role should the community play as you make your allocation decisions? How do you remain culturally sensitive when implementing this program?
2. Create a rubric to help you consider each group for inclusion in the PrEP program. What factors will you weigh in making allocation decisions? If you do not pick an entire group, what criteria do you use to select individuals in that group? How would your criteria differ if you were distributing ART drugs to infected individuals (and not to those who are at risk but not infected)?
3. What role should the likelihood of patient adherence play in your allocation decision? Keep in mind that patients are expected to take their medication daily on a strict time schedule.
4. How will you determine if your program is successful? How will you determine whether your allocation decisions are just and fair?

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8.7 Case 3: Drug Trials in Developing Countries

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8.7.1 Background

Clinical trials outsourced to India offer, in addition to business opportunities for clinical research management, the prospect of health infrastructure development and collaborative research. Since 2005, drug trials in India have increased as foreign drug companies eagerly take advantage of the favorable research environment (British Broadcasting Corporation [BBC] News 2006; Russia Today 2010; Overdorf 2011; John 2012). These advantages include highly qualified English-speaking doctors, a large and diverse population, and lower costs and relative freedom from burdensome regulations for privately funded research trials (World Health Organization 2008). As a result, clinical research organizations working on behalf of pharmaceutical companies frequently approach doctors in private or government practice to recruit patients for drug trials, often offering attractive payouts per recruit and promising coauthorship and publication credits as incentives.

For vast sections of its demographic, India grapples with inadequate access to health services and high rates of infant mortality and communicable diseases (Government of India Planning Commission 2011). Only a small slice of the population can afford the high-end private and corporate hospital care in urban pockets of the nation. Though extremely deferent to physicians, the Indian population is insufficiently informed about the risks and benefits of clinical trials. Illiterate, impoverished, and unaware of the implications of participation, many drug trial recruits are vulnerable to exploitation (Srinivasan and Nikarge 2009). With limited health care options, some gladly enroll in a drug trial, considering themselves fortunate to receive medical attention, food, and compensation for local travel. Such circumstances compromise the intent behind freely giving informed consent.

The media has drawn attention to several high-profile cases. These involved poor people from lower castes who enrolled in drug trials without adequate consent, resulting in severe adverse effects, including death (Lloyd-Roberts 2012). Citing data for 2005–2012, the BBC reported that 2,000 clinical trials took place in India. The death count among people enrolled in these clinical trials was 288 in 2008, 637 in 2009, 668 in 2010, and 438 in 2011 (Lloyd-Roberts 2012). The media also raised concerns about inadequate regulation of private trials, inconsistent application of informed consent requirements, and irregularities in ethics reviews (The Hindu 2011; The Indian Express 2012).

Although officials have been responsive to these concerns, their efforts still leave the vulnerable unprotected. In 2000, the Ministry of Health and Family Welfare established legal guidelines regulating the conduct of research in India that align with international guidelines on research ethics including the International Conference on Harmonisation of Good Clinical Practice (ICH-GCP) (1996), the Declaration of Helsinki (World Medical Association 2008) and Council for International Organizations of Medical Sciences (CIOMS) guidelines (2002). The Indian Council of Medical Research also developed guidelines specifically for clinical trials (2006). Further, the Drugs and Cosmetics Rules were amended to require review and registration of trials and to compensate trial participants or their families in the event of an adverse event (Government of India 2005). Unfortunately, adverse events go grossly underreported. Few recruits receive compensation, and hardly any investigations result in convictions for unethical research practices.

8.7.2 Case Description

Sharada, a 45-year-old woman of a low social caste in an impoverished town in India, lives on less than 2 U.S. dollars a day. She has access only to the government hospital system that provides free health care to underserved citizens. Complaining of chest pains, she is taken to the nearest government hospital and diagnosed with heart and renal failure. Pharmakon, a multinational pharmaceutical company, happens to be conducting a trial for a drug that has renal-protective effects in cardiac failure. From a colleague serving as a site investigator for this trial, Sharada's cardiologist hears that pilot testing of the drug has shown promising results. But he also learns that

his colleague's compensation is tied to the number of subjects he enrolls in the study. Worse, Pharmakon has a history of enrolling patients without ensuring they fully understand they will be participating in a research project. Despite misgivings about this history and his colleague's financial incentive to enroll patients, Sharada's cardiologist recommends that she enroll in the drug trial. He emphasizes that enrollment offers the only way to obtain an expensive drug necessary to save her life that would otherwise be unaffordable. Given the family's lack of education, he is uncertain how much they understood, yet they seem grateful for the prospect of immediate care and treatment. While on this medication, Sharada develops cardiac arrhythmias, is taken off the drug, and is discharged from the hospital in a few days. Almost a month later, she succumbs to cardiac arrest at home. Soon thereafter, the high number of serious drug-related complications forces discontinuation of the drug trial.

8.7.3 Discussion Questions

1. Who are the stakeholders in this case, what is at stake for each of them, and what values does each bring to the situation?
2. What are the risks and benefits of enrolling impoverished, uneducated patients living in developing countries in clinical drug trials? What are the barriers to obtaining true informed consent from these patients, and what can be done to overcome these barriers?
3. What are the ethical implications of tying a researcher's compensation to the number of subjects enrolled? Should this practice be permitted?
4. Are multinational pharmaceutical companies that benefit from cost-effective drug trials in developing countries obligated to improve the lives of people living in those countries?
5. Who should be held responsible for adverse events due to a drug trial conducted by a multinational company in a country where there is limited health insurance, no social security, and poor enforcement of regulations? What international or grassroots efforts might help ensure accountability for adverse events?

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8.8 Case 4: Ethical Issues in Responding to International Medication Stock-Outs

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8.8.1 Background

The World Health Organization (WHO) maintains a list, updated every 2 years, of medications it considers essential—medications that a given country should have on hand to distribute to its citizens (WHO 2015). In functioning health systems, the intent is to have essential medicines of assured quality available at all times in adequate amounts, in appropriate dosage forms, and at an affordable price (WHO 2015). Among those medications are treatments for tuberculosis (TB), a ubiquitous, slow-growing bacteria that kills 1.4 million people annually (WHO 2012).

Control of TB requires the availability of medication for months of treatment. Procurement of TB medication requires an intact and predictable supply chain. Ideally, ministries of health in low-income countries forecast accurately the number and types of medications needed to treat the local burdens of disease. Then governments typically purchase medications to store in a central facility for regional distribution. Inefficiencies in drug supply forecasting; stocking practices; storage capabilities; transportation capacity; and timely funding, procurement, and delivery can lead to a breakdown in a supply chain.

One barrier to TB control in low-resource countries, as well as in the United States, is intermittent unavailability of TB medication, an occurrence known as a stock-out (Centers for Disease Control and Prevention 2013). Medication stock-outs often result in delayed treatment, an increased risk of drug resistance in incompletely treated people, and the potential for untreated or incompletely treated people to infect others. Stock-outs occur for different reasons, including budget constraints, poor drug procurement policies and distribution networks, and political corruption slowing drug availability (Stop Stock-outs Campaign 2010).

Although 80 % of national ministries of health reporting to WHO have an uninterrupted supply of first-line TB medications, 45 % of the 20 highest-burden countries report stock-outs (WHO 2009). More recently, 14 countries experienced anti-TB drug stock-outs in 2011 (Stop TB Partnership 2011). To contend with recurrent stock-outs, the Stop TB Partnership provides technical support and drug procurement avenues to resource-poor nations through its Global Drug Facility (GDF) and Green Light Committee (GLC) (Stop TB Partnership 2011). Although GDF and GLC are essential players in ensuring at-risk nations have adequate drug supplies, both are limited in how quickly they can respond to stock-outs.

Advocacy groups and nongovernmental organizations can generate widespread public attention in hope of quicker resolution of stock-outs. A paucity of literature covers the ethical roles of expatriate health workers in stock-outs. The model of “ethics of engaged presence” in health practice for expatriate health workers in low-income countries may offer a framework of solidarity with local people (Hunt et al.

2012). This nondirective framework broadly centers on the moral dimensions of expatriate involvement in humanitarian health work undertaken with local individuals. Still, limited ethical guidelines exist for expatriates who seek to enter foreign political and social forays to affect change—leaving the problem of essential TB medication stock-outs unresolved.

8.8.2 Case Description

You are a visiting researcher in an East African country investigating TB case-finding detection strategies in an urban area. This country has one of the highest TB burdens in the world. Its government funds the national medical stores to stock anti-TB drugs per WHO's essential medication list. On occasion, you work in the TB clinic at the local hospital treating TB patients, some of whom have multidrug-resistant TB. You know that your research participants are guaranteed TB drugs through your study's funding. Potential participants who do not qualify for the study but have active TB infection are referred to a local clinic.

After months living and working in this country, you learn that many of the urban and rural clinics carry an inadequate supply of anti-TB medications. You speak with local doctors about the anti-TB drug shortage. They are frustrated and speculate as to why there have been stock-outs. Some suspect corruption and misuse of funds by the ministries of finance and health are to blame. Others blame drug manufacturers for unreliable supplies.

You search for drug stock-outs in this country using Internet search engines and come across stock-outs for other drugs but find no mention of anti-TB drug stock-outs. You return to a weekly clinic meeting and note that the news has not covered the stock-outs your colleagues are experiencing at their clinics. You ask if any of them will push the ministry of health to fix the shortage. One physician says he heard that the ministry will "provide the TB drugs again shortly." You suggest that one of the physicians contact someone from a media outlet to raise attention. After a period of silence, a physician says she fears that the government will somehow retaliate if this issue is raised.

After further conversations with colleagues, you decide to attract media attention to this issue. Your local colleagues support you, even saying they will provide you with data about the stock-out. Contacts in your U.S.-based sponsoring organization feel ambivalent about your working with the media to raise attention but will not prohibit it so long as you do not mention your affiliation.

You decide to contact an international health and human rights organization about the stock-out, and its staff puts you in touch with a local partner organization. The local partner wants you to speak, along with local human rights advocates, at a stock-out conference and interview with newspaper reporters. Despite your wanting to help those dependent on the national drug supply for their TB treatment, you are conflicted about your participation and its possible repercussions. Before committing, you tell the local partner that you need to think the matter through thoroughly.

8.8.3 Discussion Questions

1. What are some risks and benefits of your involvement with the stock-out conference and contact with the media? What ethical concepts should inform your decision? Would your decision change if your colleagues or sponsoring organization urged you to say nothing?
2. How does your limited understanding of local institutional hierarchy and governance inform your ethical analysis of whether or not to engage in advocacy around stock-outs? If you conclude you should engage, are there ways to do so besides public testimony?
3. Does it matter ethically if the stock-out pertained to antimalarial medications; that is, a medication outside your research area (TB medication)? Why or why not?
4. In terms of perceptions and consequences from the media and government ministries, how might your public reporting of the stock-out differ from a local official reporting it? What different types of impact might result from each? How might your ability to work with local health professionals in the future be affected if you report the alleged stock-out?
5. Knowing that you have ready access to anti-TB medication for research participants, should you broaden the inclusion criteria to allow more patients to receive guaranteed treatment? Why or why not?
6. Should you attempt to bring the stock-out to the attention of the global health international community by inviting members of the international media to the stock-out conference? If not, why not? If so, what approaches might international and local nongovernmental organizations, World Health Organization departments, and patient advocacy groups employ to effectively publicize and resolve stock-outs? If not, why not?
7. Do you have an ethical duty to report the stock-out if local health officers will not do so?

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8.9 Case 5: Transmitting Cholera to Haiti

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8.9.1 Background

Cholera is caused by infection with *Vibrio cholerae* bacteria, which colonize the small intestine and produce cholera toxin. The disease is characterized by sudden onset of severe, watery diarrhea and vomiting. Left untreated, cholera rapidly leads to dehydration and shock. Severe cholera can be fatal in more than 50 % of cases. Prompt treatment reduces the case fatality rate to less than 1 % (Boore et al. 2008). Treatment primarily addresses the loss of fluids: patients should be aggressively treated with oral rehydration solution or, if severely dehydrated, through intravenous fluids. Treatment with antibiotics shortens the course of the disease.

Cholera is transmitted through contaminated food or water. In developing countries, where most infections and deaths occur, inadequate sanitation is frequently the cause of the spread of *V. cholerae*, as untreated fecal matter from cholera sufferers leaks into the water supply. Each year, 3–5 million cases of cholera occur, leading to about 120,000 deaths (Harris et al. 2012).

Cholera is endemic in more than 50 countries. In many places, cholera outbreaks are seasonal—flaring up during the rainy season and dying down again during dry periods. Outbreaks can be prevented or contained by properly treating sewage, promoting rigorous hygiene practices, and sterilizing drinking water. Two oral cholera vaccines are commercially available but not included in most cholera control

programs, although the World Health Organization (WHO) recommends them for use in outbreaks and for high-risk populations (WHO 2010). Before 2010, Haiti had not experienced cholera for at least a century.

Haiti, a country of ten million people, occupies the western portion of the island of Hispaniola in the Caribbean. Although its per capita gross domestic product (GDP) is about \$1,200 (Central Intelligence Agency 2012),¹³ a tiny elite controls most of the country's wealth. With 80 % of the population living below the poverty line, Haiti is the lowest-ranked country in the Americas on the United Nations (U.N.) Human Development Index (UNDP 2011). The economy depends heavily on remittances from Haitians working abroad and on foreign aid.

Life expectancy in Haiti is 62 years, while infant mortality is 52 per 1,000 live births (UNDP 2011). Sixty-four percent of Haitians have access to an improved water source (i.e., one that is protected from outside contamination), but just 26 % have access to improved sanitation (i.e., a facility that separates human excreta from human contact) (WHO/UNICEF 2013). Communicable diseases, including HIV/AIDS, tuberculosis, diarrheal diseases, and malaria remain substantial causes of disability and death. There are severe shortages of physicians, nurses, hospital beds, and essential medicines. About 6 % of GDP is spent on health, of which three-quarters is private expenditure. Out-of-pocket spending on health care is extremely high (UNDP 2011).

Haiti has a long history of political instability, characterized by multiple coups, foreign interference and occupation, and extended periods of dictatorship, notably under François Duvalier (Papa Doc) and his son Jean-Claude Duvalier (Baby Doc) between 1957 and 1986. Following a coup in 2004, the U.N. stationed peacekeepers in Haiti. The U.N. Stabilization Mission in Haiti (MINUSTAH) has been in Haiti ever since.

In January 2010, a magnitude 7.0 earthquake struck Haiti. Hundreds of thousands of people died and up to a million were left homeless. International aid agencies, donor governments, and nongovernmental organizations (NGOs) mobilized rapidly in response, and substantial amounts of money and aid were promised to assist in rebuilding.

8.9.2 Case Description

In mid-October 2010, upstream of the Artibonite River, a sudden rush of people began presenting at the local hospital with acute diarrhea, signaling the first cholera cases. People living nearby use the river extensively for washing, bathing, and drinking water; farmers downstream use it for irrigation. Within days, the spread of cholera to the Artibonite River Delta and settlements on the coast had overwhelmed local clinics and hospitals. The facilities lacked cholera cots that allow patients to defecate hygienically from their beds, while insufficient space for all patients prevented isolation of cholera victims. For the thousands of sufferers, the supply of

¹³Purchasing power parity in 2011 U.S. dollars.

doctors, nurses, and rehydration packs proved inadequate. The epidemic exploded across Haiti. Since cholera was not endemic, the population lacked immunity. Within months, thousands of people had died and hundreds of thousands had been sickened.

NGOs and some international donor agencies, including from the U.N., who were already in Haiti dealing with the aftermath of the earthquake, diverted resources to combat cholera. They distributed medical supplies, organized educational campaigns on cholera prevention, trucked clean drinking water and water purification tablets across the country, and worked with local hospitals to institute rigorous infection control measures.

The Haitian and international response to the cholera outbreak rapidly brought the case fatality rate from around 9 % to less than 1 %. Although the outbreak died down, the aid efforts failed to rectify the dire state of Haiti's water and sanitation infrastructure. During the rainy season, cases would spike again, exposing the difficulty of improving the Haitian health care system so that it could respond to new outbreaks without external assistance.

Haiti had been cholera-free for more than a century—so how had cholera got there? Almost as soon as the outbreak started, rumors circulated blaming U.N. peacekeepers. A contingent of soldiers from Nepal, where cholera is endemic, had arrived in October 2010. They were stationed at a camp on a tributary of the Artibonite River near where the outbreak began. Waste management at the base was rumored to be inadequate and had allowed sewage to flow into the river.

Initially, U.N. officials denied responsibility for bringing cholera to Haiti. But rumors and public protest persisted, fueled by independent investigations suggesting the camp as the source (Piarroux et al. 2011). Finally, the U.N. Secretary General convened an independent panel of experts charged with determining the source of the cholera outbreak. The panel completed its report in May 2011. It argued that the evidence from the Artibonite River's tributary system, the epidemiological timeline, and genetic analyses of Haitian *V. cholerae* bacteria indicated that the outbreak resulted from contamination of the river with feces carrying a strain of the current South Asian bacterium. Moreover, the report noted that the "haphazard" plumbing construction in the main toilet and showering area offered significant potential for cross-contamination, and that heavy rains could cause the open septic pit into which black water was deposited to overflow into the tributary (Cravioto et al. 2011).

The report offered a series of recommendations to prevent similar occurrences and concluded

The introduction of this cholera strain as a result of environmental contamination with feces could not have been the source of such an outbreak without simultaneous water and sanitation and health care system deficiencies. These deficiencies, coupled with conducive environmental and epidemiological conditions, allowed the spread of the *Vibrio cholerae* organism in the environment, from which a large number of people became infected.

The independent panel concludes that the Haiti cholera outbreak was caused by the confluence of circumstances as described above and was not the fault of, or deliberate action of, a group or individual (Cravioto et al. 2011).

Since the initial outbreak, more than 7,500 Haitians have died from cholera and more than 600,000 have been sickened. Subsequent independent genetic analysis

confirmed that the Haitian strain was almost identical with the strain currently circulating in South Asia (Hendriksen et al. 2011).

Many commentators believe that the systemic deficiencies that enabled the outbreak are partly the fault of the Haitian government. It failed to take appropriate measures to protect its population from disease, such as improving drinking water and sanitation, investing in health care infrastructure, and so forth. The Independent Panel concluded that the introduction of cholera by the U.N. mission was therefore not the fault of the U.N. An alternative view is that multiple actors were at fault for this tragedy, including the Haitian government, the U.N., and foreign governments whose policies affect Haiti.

A distinct issue is whether and how the victims of the outbreak should be compensated. One option is to make compensation the responsibility of those at fault, although the difficulties in assigning fault may make this option challenging. An alternative is to establish a no-fault scheme that would compensate anyone affected, but determining who must pay is also problematic. Donors working on earthquake relief in Haiti, for example, arguably should not have to divert funds to remedy a problem they did not create. In November 2011, a legal suit was brought against the U.N. seeking compensation for the victims of the cholera outbreak (Sontag 2012). In February 2013, the U.N. invoked legal immunity against such suits and refused to provide compensation.

8.9.3 Discussion Questions

1. Which parties' interests are affected by the cholera outbreak? Which parties might have some responsibility to respond to the outbreak?
2. The U.N.'s Independent Panel of Experts concluded that "the Haiti cholera outbreak was caused by the confluence of circumstances ... and was not the fault of, or deliberate action of, a group or individual." Assume that they are correct about the facts. Does it follow that no one is morally at fault? Explain why or why not.
3. Imagine that you are providing recommendations for compensating the victims of infectious disease outbreaks, like Haiti's. Should individual actors be held accountable, or should a no-fault compensation scheme be put in place? If the latter, who should provide compensation? Explain the reasons for your responses. (Douglas 2009 discusses "no-fault" compensation in another context.)
4. If the Haitian government has neglected its responsibilities to its citizens, does this make any difference to the help that international aid agencies should provide to Haiti? Explain why or why not.
5. One possible concern with seeking compensation for the people who contracted cholera is that it may have a "chilling effect" on international assistance. For example, if aid agencies believe they are at risk of being sued for unintentionally transmitting disease, they may be deterred from working in a country in the first place. Should the Haitian government or the lawyers representing the victims take this concern into account? Why or why not?

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8.10 Case 6: Perilous Path to Middle East Peace: The Sanctions Dilemma

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8.10.1 Background

During the last century, public health practices have greatly improved the health of individuals and societies in the Middle East and North Africa (MENA) region through successful interventional programs like expanded immunization for children and universal salt iodization programs. The major challenge for public health in the twenty-first century is to simultaneously maintain and upgrade the infrastructure created to improve peoples' lives.

Currently, the MENA region faces multiple challenges to its public health achievements, one of which is the impact of sanctions being used against MENA countries to influence political behavior. Sanctions—defined as mostly economic but also political and military penalties introduced to alter political/military threats and behavior—are employed by the United States and other countries to discourage the proliferation of weapons of mass destruction and ballistic missiles, bolster human rights, end terrorism, thwart drug trafficking, discourage armed aggression, promote market access, protect the environment, and replace governments (Haass 1998). Sanctions often involve economic measures, such as restricting or eliminating foreign assistance, freezing countries' assets, imposing export and import limitations, and revoking most-favored-nation trade status (World Health Organization 2003).

Empirical evidence indicates that sanctions have profound long- and short-term public health impact on the health of citizens in the affected countries, with the greatest harm affecting the elderly, women, and children (Garfield 1999; Ali and Shah 2000). This impact goes far beyond problems with medical supplies or other health-specific resources. Public health services depend on a safe water supply, a functioning sanitation system, and a reliable power infrastructure; on availability of equipment such as ambulances, X-ray machines, and refrigerators for storing vaccines; on the public having resources to access health care (e.g., transportation, financial resources); and on human resources, the trained staff who use the equipment.

Two examples of the use of sanctions were those imposed by the United Nations (U.N.) against Iraq in the 1990s and against Syria beginning in 2011.

8.10.2 *The Case of Iraq*

To assess the health impact of the Iraq sanctions, the U.N. Children's Fund (UNICEF), in collaboration with the World Health Organization and local health authorities surveyed child health in Iraq during February through May 1999 (UNICEF 1999a, b). Between 1984 and 1989, infant mortality in Iraq was 47 per 1,000 live births (Ali and Shah 2000). In southern and central Iraq, the infant mortality rate almost tripled, rising to 108 per 1,000 live births during 1994 through 1999. The under-5 child mortality rate also drastically increased (more than doubled) from 56 to 131 per 1,000 live births for the same period (Ali and Shah 2000). Yet in the autonomous northern region of Iraq, infant mortality declined from 64 to 59 per 1,000 live births and under-5 mortality fell from 80 to 72 per 1,000 live births for the same period. These differences were attributed to better food and resource allocation due to Western support for an autonomous region and the nonapplication of universal sanctions (UNICEF 2002).

Other studies of the health impact of sanctions on Iraq have similar negative findings (Armijo-Hussein et al. 1991; Hurwitz and David 1992; Central Statistical Organization, Iraq 1996, 1997). Table 8.1 summarizes data from these studies and shows the change in health indicators once sanctions were imposed in 1990.

8.10.3 *The Case of Syria*

Since May 2011, economic sanctions against Syria significantly affected the exchange rate, devaluing its Syrian Lira (SL). The exchange rate of 45 SL for every U.S. dollar increased to more than 200 SL and had serious economic ramifications. The cost of living essentials such as gas, eggs, milk, bread, and cooking oil more than tripled over the past 2 years. At the same time, the purchasing power of

Table 8.1 Health status indicators before and after the 1990 sanctions against Iraq

Indicator	1985	1991	1996
Infant mortality rate	52	42	97
Under-5 mortality rate	64	42	126
Chronic malnutrition (%)	18	18	32
Stunting (%)	12	29	26
Maternal mortality per 100,000 births	–	121	294
Diarrhea episodes per child per year	–	3.8	14.4
Births below 2.5 Kg (%)	5–9	4.5	12

Note. A dash indicates that reliable data are not available

salaries was halved. Families, nearing starvation, were forced out of work, and more than 20 % of the working population was unable to purchase living essentials (Zarzar 2013; Food and Agriculture Organization of the United Nations 2013). The collapse of the exchange rate increased the cost of health services and of medicines. Despite the emphasis of sanctions on economic measures, they prevented entry of essential medical supplies into the country, including those for chronic diseases such as cancer, diabetes, and heart disease, which are not produced locally. Local drug production, an area in which Syria had been 90 % self-sufficient before the sanctions and conflict, largely collapsed. This opened channels for counterfeit drugs and corruption among those who smuggled supplies through the country's porous borders. The high cost of heating and electricity during 2 years of conflict compounded the adverse effects of Syria's extreme winter and summer temperatures. Most notably, the cold chain of vaccines were destroyed, contributing to the virtual collapse of the once successful vaccination programme (Al Faisal et al. 2012a, b). The combination of price increases, job losses, and lower salaries devastated families, especially those with children or members who were pregnant or elderly (United Nations Office for the Coordination of Humanitarian Affairs 2013). Millions of small businesses collapsed in Syria. Many were small-scale and home-based, run by women providing invaluable income to cope with price inflation and to purchase food, school books and uniforms for children, and essential medicines and emergency medical care.

8.10.4 Ethical Considerations

Before World War I, economic sanctions were considered acts of warfare that, like military sieges, inflicted suffering on entire populations. Viewed this way, economic sanctions appear ethically suspect from a number of perspectives. Sanctions violate the just war ban on targeting noncombatants, the Kant's philosophy not to use people as means to an end, and the negative right of populations not to be deprived of their means of subsistence (Gordon 1999; United Nations 2005). However, after World War I when the League of Nations was created, economic sanctions came to be viewed as a peaceful, diplomatic alternative to war that could prevent military intervention (Gordon 1999). This viewpoint holds that to justify sanctions, the benefits of avoiding the presumably far greater harms caused by war, civil war, or long-term political oppression must outweigh the harms sanctions impose on a populace. But this grim utilitarian calculus must also consider the probability of the success of sanctions, which generally is low. Pape (1997), for example, estimates that sanctions lead to political compliance less than 5 % of the time. More optimistically, Hufbauer et al. (2009) judge sanctions effective in 34 % of situations used. However, they stress that the success of sanctions depends on many factors including the purpose; the relative economic instability of the country receiving sanctions; whether the country receiving sanctions is part of a broad array of diplomatic, economic, military, and covert measures; and whether the sanctions are being imposed in the context of a broader international coalition (Hufbauer et al. 2009).

8.10.5 Case Description

You are a public health official from a country in the Middle East researching the impact of economic sanctions on the health of populations. You have seen first-hand the impact sanctions have had on vulnerable populations. You also have expertise in public health ethics and have written extensively about ethics in the use of economic sanctions. You have been invited by a United Nations commission to testify on the health impact of sanctions. The commission values your opinion on whether sanctions are ever ethical and justified.

8.10.6 Discussion Questions

1. What are the range of ethical considerations for and against the use of economic sanctions? Are there ways of imposing economic sanctions that can avoid forms of collective punishment and minimize subsequent adverse health impact on individuals and populations?
2. In extreme situations where many human lives are at stake, such as emergency disaster relief, doctors and public health officials often revert to simple utilitarian calculations of lives lost or saved (e.g., triage decisions). To what extent is the ethical logic surrounding economic sanctions similar or dissimilar to the ethical logic of emergency disaster relief?
3. Can economic sanctions be ethically justified
 - (a) as an alternative to long-standing political oppression and human rights violations?
 - (b) to prevent civil war?
 - (c) to avert war?
 - (d) to effect regime change?

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8.11 Case 7: Advancing Informed Consent and Ethical Standards in Multinational Health Research

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This case is presented for instructional purposes only. The ideas and opinions expressed are the authors' own. The case is not meant to reflect the official position, views, or policies of the editors, the editors' host institutions, or the authors' host institutions.

8.11.1 Background

In the United States, regulations for informed consent largely came about during the 1950s through 1970s not only in response to unethical human experiments carried out in Nazi Germany, but also to those within U.S. borders (Beecher 1966). Experiments like the U.S. Public Health Service Tuskegee Syphilis Study (Jones 1981) prompted Congress to enact human research regulations, initially through the 1974 National Research Act. Subsequently, other research guidelines have been developed and revised (World Health Organization 2000; Council for International Organizations of Medical Sciences 2002; The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use 1996; World Medical Association 2008), fostering expansion of ethics commissions and review boards and making informed consent an integral component of health research (Meslin and Johnson 2008). Yet, half a century later, many countries still lack adequate human research regulations or regulatory authorities. These regulatory gaps leave research participants, their families, and communities at risk for great harm through sociocultural discrimination, research-related illness, disability, and death and post-experimental medical abandonment. In Nigeria, Pfizer tested an unapproved drug on infants and children (Abdullahi v. Pfizer Inc. 2002); in India, Johns Hopkins tested cancer drugs on patients without proper consent (Sharma 2001); and other such incidents have been reported (LaFraniere et al. 2000). Even the U.S. National Institutes of Health failed to produce consent forms for experiments on HIV-positive women in developing countries (Public Citizen 1998).

On a practical and ethical level, debate continues over human research and informed consent (Tri-Council 2010; Marshall 2008; Nuffield Council on Bioethics 2002). While some argue for a single ethical standard for human research (Lurie and Wolfe 1997; Angell 1997), others believe that imposing a global ethical standard irrespective of cultural differences would amount to ethical imperialism (Resnik 1998). *The New England Journal of Medicine* “has taken the position that it will not publish reports of unethical research regardless of their scientific merit” (Angell 1997). But like other scientific journals, it has found difficulty in determining what is unethical versus what is culturally appropriate research in different settings.

There are many challenges to obtaining informed consent. Some involve illiteracy; noncomprehension of information; language and communication barriers; or unfamiliarity with certain scientific, medical, or ethical concepts. Other challenges are attributable to complex sociocultural, psychological, or structural elements, such as shared decision making by community members, rather than by an individual (Marshall 2000, 2008). Some studies, however, take the stance that such challenges do not preclude an individual's ability to understand or voluntarily participate in research studies (Pace et al. 2003). Consequently, in order to ensure that research participation is voluntary, it is important to safeguard a participant's right to refuse or withdraw from a study at any time.

One practical solution to obtaining appropriate consent is by implementing culturally acceptable methods such as oral consent, video documentation, or community meetings (Tri-Council 2010; Nuffield Council on Bioethics 2002; Dawson and Kass 2005). Another is to require foreign researchers to receive dual approval through a local review board and their own institutional review board (IRB) (World Health Organization 2000; Council for International Organizations of Medical Sciences 2002; Tri-Council 2010). Nevertheless, multinational collaborations in research, especially those originating in regions that lack adequate research regulations, can be problematic because research "approval" may not provide adequate protections.

De-identified data and information¹⁴ pose an additional complication for obtaining proper informed consent. These can include "x-rays, endoscopic images, images of organs or tissues taken during an autopsy, still or video recordings of surgical procedures, and microscopic images" (Tranberg et al. 2003). As long as these remain de-identified, researchers need not obtain informed consent (European Union 1995; U.S. Department of Health and Human Services 2009; National Institutes of Health 2007). However, in countries lacking adequate research ethics infrastructures, waiving informed consent is problematic at several levels. First, verifying if appropriate consent was obtained becomes virtually impossible. Second, the lack of consent can be medically dangerous for research participants and have legal repercussions for researchers (Flory et al. 2008). Finally, it can complicate the research process by compromising the utility of research samples and data (Wendler 2008).

Continued globalization, international development and increased accessibility to data through electronic medical records and online databases will increase multinational human research. As multinational research becomes more common, the need to find appropriate ethical standards and informed consent policies will become more urgent. Ultimately, the goal of such standards and policies should be to ensure that research participants and their information are safeguarded at the origin and throughout every step of the research process.

¹⁴De-identification involves stripping data and information of personal identifiers (e.g. names, addresses, birth dates, photos, or any unique identifiers), such that an individual's identity remains anonymous and cannot be retraced.

8.11.2 Case Description

You are an infectious disease specialist working at a university in a high-income country and are interested in researching cervical cancer in immunocompromised patients. Because you collaborate regularly with colleagues worldwide, other researchers commonly seek your input. An African colleague e-mails you for advice on a multinational cervical cancer study she is conducting with several other researchers in seven different African countries. This study began 3 years ago to address the local population's health needs and has been funded by local hospitals and organizations. This colleague, a public health professional, has compiled the research data in an online database. The information she sends you includes an electronic copy of the preliminary report, de-identified data set, and pathology slides of cervical specimens. After reviewing her preliminary findings, you agree that her research could positively impact the health outcomes of individuals in her community.

Excited by this initial review, your colleague invites you to coauthor an upcoming manuscript on the study. You carefully review the methods section of the preliminary report, focusing on how consent was obtained. In one research country, consent was provided via video documentation; in two others, it was obtained through a standardized consent form; and in a fourth, through verbal consent of male community leaders *before* seeking consent from individual participants, a practice in line with local cultural norms. For the remaining three countries, no consent documentation exists.

You follow-up with your colleague about the various consent methods. She indicates that none of the countries involved in the project have IRBs or national research guidelines, but that consent methods were typical for research projects in these countries. Regarding the three countries lacking consent documentation, she believes that some form of consent was obtained from the research participants, although she lacks supporting evidence.

Although the information you received was de-identified, you wonder about the lack of uniformity in the consent process but attribute it to respect for differing cultural norms. Based on all information provided, you believe the research has scientific merit and the data collected is scientifically valid. You also believe the study should be published, as it could significantly improve the health of the region and advance future research.

8.11.3 Discussion Questions

1. Who would you turn to in your institution for guidance regarding your involvement in the research, coauthorship of the manuscript, and other contributions to this research study?
2. What are some appropriate ways to obtain informed consent when conducting research in areas with culture or language different from yours? Name some pros and cons to each approach.

3. Does the use of multiple methods to obtain consent raise questions about the reliability of the data or validity of the research project? Without confirmation of informed consent, would you consider the publication of this research study to be scientific misconduct?
4. What are some appropriate ways to obtain informed consent for research conducted in countries with different consent standards and requirements? Are there instances when one set of requirements should take priority over another?
5. Given the multiple methods used to obtain consent, are you willing to coauthor your colleague's paper? Why or why not?

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